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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,916	07/09/2001	Hiroshi Shiku	P20854	1184

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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/787,916	SHIKU ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13,14 and 27-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,14 and 27-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 9/08/06 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's amendment and remarks, filed 9/08/06, have been entered.

2. Claims 13, 14, and 27-37 are being acted upon.

3. Applicant again requests that the previously submitted Japanese language documents be considered. Applicant is advised that absent certified translations, or concise explanations of the relevance of the information presented in the documents to the claimed invention, said documents cannot be considered.

4. In view of Applicant's amendment canceling all product claims the previous rejection under 35 U.S.C. 102(b) as being clearly anticipated by Kohno et al. (1996), as well as all rejections under the first and second paragraphs of 35 U.S.C. 112, have been withdrawn.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 13, 14, and newly added Claims 27-36, stand/are rejected under 35 U.S.C. 103(a) as being unpatentable over Nestle et al. (1998, IDS) in view of Gu et al. (1997, IDS).

As set forth previously, Nestle et al. teaches a method for inducing cellular immunity comprising isolating a DC APC, reacting said APC with a tumor antigen, and returning the resulting cell to the living body by parenteral administration (see particularly Methods, page 331, column 2 - page 332, column 1).

The reference differs from the claimed invention only in that it does not teach an APC loaded with the ErbB-2 antigen by reacting with a complex comprising a hydrophobized polysaccharide comprising mannan or a polysaccharide comprising the limitations of Claim 4 wherein the sterol is cholesterol.

Gu et al. teaches that a cholesterol bearing mannan polysaccharide complexed to an ErbB-2 antigen (an antigen overexpressed in a wide range of human adenocarcinomas, see Abstract) can be used to induce CD8+ CTLs (page 19, column 2, second full paragraph and page 23, column 1) by a mechanism of facilitating the entry of the antigen into the MHC Class I pathway for presentation by APCs (see particularly page 24, column 1, first full paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce a product for, and perform a method for, inducing cellular immunity comprising isolating a DC APC, reacting said APC with a tumor antigen, and returning the resulting cell to the living body by parenteral administration, as taught by Nestle et al. One of ordinary skill in the art at the time of the invention would have been motivated to employ the cholesterol bearing mannan polysaccharide complexed to an ErbB-2 antigen of Gu et al. given the teachings of the reference that the ErbB-2 antigen is overexpressed in a wide range of human adenocarcinomas (and would thus provide an obvious target for immunotherapy) and that the use of the cholesterol bearing mannan polysaccharide facilitates the entry of the antigen into the MHC Class I pathway for presentation by APCs.

Applicant's arguments, filed 9/08/06, have been fully considered but they are not persuasive. Applicant argues that Nestle et al. employs a peptide [antigen] cocktail, and further, the reference teaches a "need" for multiple peptides, whereas in both Gu et al publications a single peptide antigen is employed. Accordingly, Applicant argues that the skilled artisan would not be motivated to combine the references.

It is the Examiner's position that while the primary reference, Nestle et al., teaches a usefulness (rather than a "need" as characterized by Applicant) for the use of multiple peptides, in view of either Gu et al. reference the skilled artisan would have been motivated to employ an ErbB-2 antigen as one of said peptides or antigens.

Applicant asserts unexpectedly good results of the instantly claimed invention.

As set forth previously, it is well-established that it is inappropriate to assert superior or unexpected results not disclosed in the specification in an attempt to overcome an art rejection.

7. Claims 13, 14, and newly added Claims 27-37 stand/are rejected under 35 U.S.C. 103(a) as being unpatentable over

Nestle et al. (1998, IDS) in view of Gu et al. (1998, of record).

As set forth previously, Nestle et al. has been discussed above.

The reference differs from the claimed invention only in that it does not teach an APC loaded with antigen (ErbB2 also known as HER2) by reacting with a complex comprising a hydrophobized polysaccharide comprising mannan or pullulan, or a polysaccharide comprising the limitations of Claim 4 wherein the sterol is cholesterol.

Gu et al. teaches that a cholesterol bearing mannan or pullulan polysaccharide complexed to a HER2 antigen (see Materials and Methods) can be used to induce CD8+ cellular immunity (see particularly Figures 1 and 4), while antigen alone is ineffective, by a mechanism of facilitating the entry of the antigen into an APC through a carbohydrate-recognizing receptor such as DEC-205, and entry into the cytosol (for transport to MHC Class I) after phagocytosis (see particularly page 3389, column 2-3390).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce a product for, and perform a method for, inducing cellular immunity comprising isolating a DC APC, reacting said APC with a tumor antigen, and returning the resulting cell to the living body by parenteral administration, as taught by Nestle et al. One of ordinary skill in the art at the time of the invention would have been motivated to employ the cholesterol bearing mannan or pullulan polysaccharide complexed to a HER2 antigen of Gu et al. given the teachings of the reference that hydrophobized polysaccharide-antigen complex facilitates the entry of the antigen into an APC through a carbohydrate-recognizing receptor such as DEC-205, and entry into the cytosol (for transport to MHC Class I) after phagocytosis, for superior antigen presentation and cellular immunity.

This rejection has not been traversed separately.

8. The following is a new ground of rejection.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 27 and 37 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter

rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) The method … wherein the complex consists essentially of a hydrophobized polysaccharide and an antigen (Claim 27).

B) The method … wherein the antigen consists of a polypeptide consisting of residues 1-147 of ErbB-2 fused to a histidine hexamer at the N-terminal. (Claim 37).

Applicant indicates that support for the new limitations of Claim 27 can be found in the Examples. Applicant cites support in the canceled claims for the limitations of Claim 37.

Regarding A), the Examples disclose only a specific composition comprising a specific hydrophobized polysaccharide combination (a cholesterol-modified mannan and pullulan) and a specific antigen (human ErbB-2) and not the generic complex employed in the claim.

Regarding B), Example 1 disclose only a specific composition comprising a specific hydrophobized polysaccharide combination (a cholesterol-modified mannan and pullulan), i.e., not the generic hydrophobized polysaccharide of the claim. Further, the Example discloses only a polypeptide consisting of human ErbB-2 and not the generic ErbB-2 employed in the claim, and then this polypeptide is not disclosed as used in the generic method of inducing cellular immunity. The complex of the Example is employed only *in vivo* employing BALB/c mice or *in vitro* employing human peripheral blood monocytes.

11. Claims 13, 14, and newly added Claims 27-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kohno et al. (1996, of record) in view of Gu et al. (1997, of record), Nagarkatti et al (1990), and Terao et al. (1995).

Kohno et al. teaches the *in vitro* stimulation of Th1 CD4+ T cells, including increased production of IFN-γ, by DC APC capable of inducing cellular immunity, said cell having been produced by reacting *in vitro* with the hydrophobized polysaccharide pullulan and an antigen (see particularly page 213, column 1 and Figure 2).

The reference differs from the claimed invention only in that it does not teach a method of inducing cellular immunity *in vivo* nor the use of the ErbB-2 antigen.

Gu et al. (1997) teaches that ErbB-2 is overexpressed in a wide range of adenocarcinomas (see particularly the Abstract).

Nagarkatti et al. (1990) teaches that Th1 CD4+ T cells can mediate tumor rejection (see particularly, Table V).

Terao et al. (1995) teaches that Th1 CD4+ T cells expressing IFN-γ can be used in anti-tumor immunotherapy, particularly against poorly immunogenic tumors (see particularly page 146, *The anti-tumor activity of MH2 against three tumor cell lines*, and page 150, column 2).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to induce cellular immunity by the *in vitro* stimulation of Th1 CD4+ T cells, including increased production of IFN-γ, by DC APC capable of inducing cellular immunity, said cell having been produced by reacting *in vitro* with the hydrophobized polysaccharide pullulan and an antigen, as taught by Kohno et al., employing the ErbB-2 antigen which is overexpressed in a wide range of adenocarcinomas, as taught by Gu et al. The ordinarily skilled artisan would have been motivated to employ the Th1 cells produced by the claimed method in immunotherapy, i.e., administering to a patient to induce cellular immunity, given the teachings of Nagarkatti et al., that Th1 CD4+ T cells can mediate tumor rejection, and Terao et al. that Th1 CD4+ T cells expressing IFN-γ can be used in effective anti-tumor immunotherapy, particularly against poorly immunogenic tumors.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

14. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Additionally, the Technology Center receptionist can be reached at (571) 272-1600.

11/20/06

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